

Unit 2: Adult Stem Cells, Homeostasis and Regenerative Medicine

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California State Standards

Biology/Life Science

- 1.a. Students know cells are enclosed within semi-permeable membranes that regulate their interaction with their surroundings.
- 4.d. Students know specialization of cells in multi-cellular organisms is usually due to different patterns of gene expression rather than to differences of the genes themselves.
- 9. As a result of the coordinated structures and functions of organ systems, the internal environment of the human body remains relatively stable (homeostatic) despite changes in the outside environment.

Investigation and Experimentation

- 1.k. Recognize the cumulative nature of scientific evidence.
- 1.m. Investigate a science-based societal issue by researching the literature, analyzing data, and communicating the findings.

Goals

- Understand the difference between adult and embryonic stem cells.
- Understand the diversity of adult stem cells and their functions in the body.
- Understand how adult stem cells assist in homeostatic regulation in the body.
- Understand how current research of adult stem cells translates to drug development and cell-based therapies.

Objectives

1. Students will be able to demonstrate adult stem cells' role in regeneration in other animal species.
2. Students will be able to demonstrate where adult stem cells are located in the body and realize that we may discover more types of stem cells in the future.
3. Students will be able to describe homeostasis.
4. Students will be able to explain the role of adult stem cells in homeostatic maintenance of the body.
5. Students will be able to explain the difference between embryonic stem cells, adult stem cells, and progenitor cells.
6. Students will be able to research what adult stem cell therapies already exist and which are in clinical trials.
7. Students will be able to identify the steps of a clinical trial and why this process is relevant to regenerative medicine.
8. Students will be able to distinguish between therapies evaluated by clinical trials and those that have not been.

UNIT OUTLINE

I. Invitation

A. What do starfish arms, lizard tails, and your liver have in common? After reading the SYNOPSIS of the Myth of Prometheus (below) to students, discuss the myth using the following questions:

1. Prometheus (bird eats liver every day, then liver re-grows every night)
 - a. What is the purpose of the liver, and why does it regenerate?
 - b. Is this myth proof that the Greeks knew about liver regeneration?
2. Read article with graphics about the myth: Prometheus myth...busted?

SYNOPSIS:

Epimetheus and Prometheus, Titans, aid Zeus in a war against Atlas and the rest of the Titans. Zeus wins and grants the two Titans the ability to create creatures to populate Earth. Epimetheus gives strength and flight to animals—leaving no good attributes for men. Prometheus gives men the ability to walk upright, and to look towards Olympus. He also gives men fire, but tricks Zeus into accepting the inedible parts of animal sacrifices. Zeus, angered at Prometheus, takes fire away from Man, but Prometheus steals it back. Zeus punishes Prometheus by chaining him onto the Andes Mountains and having an Eagle eat his liver every day. Prometheus' liver grows back every night. Zeus finally takes pity and allows Chiron (an immortal Centaur in

excruciating pain from Heracles' poison arrow) to sacrifice himself for Prometheus' freedom, and Heracles kills the eagle.

B. What cells in your body are responsible for regeneration?

1. Where are they? Survey what students think. Use anatomically-correct black line masters of male and female bodies and record student answers, or do this on the board. Black Line Masters
2. Discuss results of this survey as a class.
 - a. For beginning students, it is safe to say that there are "regenerative" cells EVERYWHERE in the body .
Mention the major adult stem cell types: hematopoietic, mesenchymal, and neural.
 - b. For more advanced students, you can discuss hematopoietic, mesenchymal, neural, endothelial, and epithelial (etc.) stem cells and locations from the Teacher Background Information section or the supplementary PowerPoint.
3. Discussion following reading of article summaries (below).
Are there any putative stem cell populations? Where haven't we found all of the body's stem cells? Do all stem cells participate in regeneration?
 - a. Horizontal basal cells in the Olfactory bulb
Abstract and summary of text
 - i. Which type of olfactory bulb cell is controversial? Why?
 - b. Pancreatic stem cells discovered in 2008
 - c. CIRM Feature: Sights on a Cure
4. AP extension: How do scientists identify stem cells? What are the characteristics of a stem cell? Use above papers/summary and Wikipedia - Stem Cell (an excerpt, Identification, is below) to answer these questions.

Identification:

An adult stem cell is a type of cell that has the potential to regenerate tissue over a lifetime. For example, in Leukemia, the presence of hematopoietic stem cells (HSCs) in the bone marrow means that a donor has the ability to transplant their stem cells and save an individual without healthy HSCs. In this case, a stem cell must be able to produce new blood cells and immune cells over a long time, demonstrating potency. It should also be possible to isolate stem cells from the transplanted individual, which can themselves be transplanted into another individual without HSCs, demonstrating that the stem cell was able to self-renew. Properties of stem cells can be illustrated in vitro , using methods such as clonogenic assays, where single cells are characterized by their ability to differentiate and self-renew. As well, stem cells can be isolated based on a distinctive set of cell surface markers. However, in vitro culture conditions can alter the behavior of cells, making it unclear whether the cells will behave in a similar manner in vivo. Considerable debate exists whether some proposed adult cell populations are truly stem cells.

C. Discuss similarities and differences between wound healing and regeneration.

1. Watch Howard Hughes Medical Institute lecture Adult Stem Cells and Regeneration (see SYNOPSIS below)
 2. Use handout (student worksheet) while students watch the lecture. See teacher version for answer key.
- Appendix A: Student worksheet
Appendix A: Teacher version

SYNOPSIS:

Wound healing uses blood clotting factors (CF's) and hormone/protein signals, like Thrombin, to recruit layers of platelets. These non-stem cells (they are actually pieces of immune cells) clog the wound, allowing the dermis/capillary to re-grow over the wound. This re-growth can use stem cells, but isn't largely due to stem cell division. (Note: adult stem cells support the constant generation of new cells to replace old, damaged, and dying cells. They also participate in injury repair; for example, when muscle is injected with snake venom, muscle satellite cells [stem cells] divide, migrate to the injury site, differentiate, and fuse together to form new muscle fibers.) Regeneration can occur due to a limb being severed (as with the newt) or from chemical degradation (as in the liver). In limb regeneration, the wound first heals, then a blastema (group of cells) forms, inside of which are differentiating stem cells. In this way, stem cells begin to reform the regenerating body part. Thus, regeneration rather than wound healing relies much more heavily on stem cell division and differentiation, coupled with molecules which signal regeneration to occur.

II. Exploration

A. What are some different types of stem cells? Study adult vs. embryonic stem cells.

Interactive animation from Learn Genetics, University of Utah

Note: Fetal stem cells are not typically considered pluripotent nor are they equivalent to embryonic stem cells. Please clarify this with your students.

As they are, adult stem cells are able to produce one or several types of mature cells rather than all or many types of cells. Remember, pluripotent embryonic stem cells can produce most types of cells, except for extra-embryonic cells and placental cells; totipotent embryonic stem cells can produce every type of cell, including extra-embryonic cells and placental cells.

- a. Muscle stem cells cannot create blood, whereas embryonic stem cells can become anything up to a certain point in their development.
- b. Differences between stem cells and progenitor cells
 - i. Think of adult stem and progenitor cells as having different levels of potential, based on how many different types of cells they are able to become.
 - ii. In reality there is a continuum of plasticity/potency, and scientists have named and characterized just some of the discrete levels.
 - iii. An adult stem cell is generally multipotent, while a progenitor cell is generally uni- or bi-potent.

B. Homeostasis

1. What is homeostasis?
 - a. Interactive animation from BBC
 - b. Discussion question: How are these types of homeostasis (e.g., the body's thermostat, glucose/insulin hormone) different from the maintenance of cell numbers in tissue homeostasis?
 2. Describe adult stem cells' role in human tissue homeostasis.
 3. Planaria regeneration lab
 - a. Watch video: "Planarian Regeneration and Stem Cells" from Potent Biology: Stem Cells, Cloning, and Regeneration, Howard Hughes Medical Institute holiday lectures 2006. (See SYNOPSIS below.)
 - i. Use student questions that go with the video: "Planarian Regeneration and Stem Cells Video Handout"
- Appendix B: student worksheet
Appendix B: teacher version

SYNOPSIS:

This video describes the basic biology of Planaria. They have the ability to regenerate any part of its body, down to when it's cut into 279 fragments. Neoblasts (totipotent stem cells) migrate to areas of damage and create specific differentiated cells in order to regenerate the damaged parts of its body. RNAi experiments portray 240 genes involved in regeneration. One molecule, *smadwe*, is found in *Drosophila* stem cells and is involved in gonad cell function in female fruit flies. Without this protein, the Planaria die because the head begins to curl inward. In the future, these experiments using planaria can identify gene function in humans and vertebrates.

- b. Discussion questions:

Are human adult stem cells equivalent to planaria neoblasts? Do they have the same potential?

 - i. No, planaria neoblasts can regenerate the entire organism while adult stem cells in humans are restricted to regenerating tissue-specific lineages.
- c. Planaria wet lab: use the Northwest Association for Biomedical Research intro PowerPoint, lab protocol, and handouts within their Stem Cell Curriculum:

Materials for NWABR planaria regeneration lab

 - i. The brown planaria, *Dugesia tigrina*, and black planaria, *Dugesia dorotocephala*, can be purchased from commercial supply houses, such as Wards.

C. Regenerative Medicine: What is it?

1. Treating injuries and diseases using adult and pluripotent stem cells. Check out CIRM's accomplishments in this area.
 2. Jigsaw activity: What are examples in the natural world of regeneration? How do humans compare in their ability to regenerate? What cells play a role in lizard tail regeneration? What is the goal of regenerative research and medicine?
 - a. Lizard tail and salamander limb regeneration
- EASY: Limb regeneration
MID: Caudal autotomy
MID: Mice that regrow organs
MID: Regeneration quote
MID: Regeneration research revolution
MID: Heart regeneration
CHALLENGING: Research on salamander limb regeneration
CHALLENGING: Discover Magazine - How to grow a new limb

D. What are the potential uses of adult stem cells? Students should do research and take notes in a Double Entry Journal.

Appendix C: Instructions for journaling

1. Adult stem cell-based therapies that exist today

Adult stem cell therapies - Bone marrow transplant

2. Drugs that affect or target stem cells

Breast cancer drug

3. Using stem cells to test/screen drugs in vitro

Drug screening

4. Potential uses of stem cells

Diagram and article from HealthlineNews

E. Process and importance of clinical trials

1. Explain steps in clinical trials (preclinical through phase 4). See Teacher Background Information section and associated web readings and resources (listed below).

2. Also use the Student handout "Clinical trials information chart" and see the teacher version for answers.

Appendix D: Student worksheet

Appendix D: Teacher version

3. Web resources

MID: Stem cell drugs/therapies next big market

MID: Dose-response relationships

MID-CHALLENGING: Clinical trial design

MID-CHALLENGING: The Valley of Death

CHALLENGING: FDA Article

III. Application

A. Clinical trial exercise

1. Use Regenerative medicine and clinical trials research project instructions and grading rubric:

Appendix E: Instructions

Appendix E: Grading rubric

2. Students choose diseases from 70+ diseases

Appendix F: Disease list

3. Students complete preliminary research forms

Appendix G: Blank forms, sample form, actual student logs

How many hits, general type of therapy (cell-based, drug, etc.) Find any stem cell therapies on the market for these diseases (there may not be an example.)

4. Narrow down to one disease. Answer questions on Instructions handout.

5. Use the information found to create a PowerPoint presentation summarizing the clinical trial results from chosen disease.

Appendix H: Student examples: HIV, Macular Degeneration, Spinal Cord Injury

OR

B. If you were an adult stem cell, what kind would you be?

1. Write an essay explaining why you are important, where you "work," and a detailed description of how you keep the body healthy and homeostatic.

OR

2. Draw the questions in B.1. as a cartoon/storyboard.

OR

3. Or create a pamphlet about why people should know about your certain type of adult stem cell.

IV. Assessment

A. Name three different types of stem cells.

B. Fill out the characteristics of embryonic and adult stem cells vs. progenitor cells table:

Appendix I: Student assessment

Appendix I: Teacher rubric

C. What is homeostasis and why is it important to living organisms?

D. Where have we found adult stem cells?

E. Why are scientists studying newt (or planaria) regeneration in relation to human limbs?

F. Why do we need adult stem cells?

G. What are some of the current uses of adult stem cells?

H. What are the steps in clinical trials and what do they mean?

Additional Resources

Check Medical News Today, Wired.com, New Scientist, ScienceDaily to stay current.

Learn Genetics Stem Cell Animations

Harvard resources on stem cells and regenerative medicine includes lesson plans, scientific animations, and scientist lecture videos plus lessons for students learning English

Howard Hughes Medical Institute's activities and animations

Clinicaltrials.gov: Understanding Clinical Trials

From Idea to Market: The Drug Approval Process

Eye Cells Believed To Be Retinal Stem Cells Are Misidentified

Grow Limbs for Soldiers

Info and pictures about lizard tail regeneration (EASY)

Stem cell info from the National Institutes of Health

Interactive physiology animation about homeostasis

Restoring vision using retinal stem cells video

General stem cell videos from Howstuffworks

Researchers Identify Major Source of Muscle Repair Cells: Implications For Treating
Duchenne's Muscular Dystrophy

Source URL: <https://www.cirm.ca.gov/our-progress/unit-2-adult-stem-cells-homeostasis-and-regenerative-medicine-0>